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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,840	07/27/2001	Alfred M. Handler	0203.00	7175

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EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

DATE MAILED: 05/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/915,840	<b>Applicant(s)</b> HANDLER, ALFRED M.	
	<b>Examiner</b> Gerald G Leffers Jr., PhD	<b>Art Unit</b> 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 17 February 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 6-8 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 9-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>7/27/2001</u> . | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Election/Restrictions***

Applicant's election with traverse of Group I (claims 1-5, 9-19) in the response filed 2/17/2004 is acknowledged. The traversal is on the ground(s) that there would not be a serious search burden in examining both groups together. This is not found persuasive because the invention of Group II (claims 6-8), directed to transgenic animals, requires additional searching not required for the invention of Group I (e.g. enablement issues with regard to the making of transgenic animals).

The requirement is still deemed proper and is therefore made FINAL.

### ***Petition for Color Photographs***

Receipt is acknowledged of a petition, filed 5/12/2003, for the acceptance of color drawings in the instant specification. The examiner is currently in the process of obtaining the color drawings from the storage facility. A decision on the proposed drawings will be made once the drawings are obtained. It is noted that neither the specification nor the petition appear to comprise the required paragraph concerning the availability of copies of the color drawings. An amendment of the specification to include the following language as the first paragraph of the brief description of the drawings section of the specification is required:

The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

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***Information Disclosure Statement***

Receipt is acknowledged of an information disclosure statement filed 7/27/2001. The signed and initialed PTO Form 1449 has been mailed along with this action. U.S. Application Serial No. 09/377,066 has been considered, but has been lined-through on the PTO Form 1449 as it is not intended for printing on the face of any patent to issue from the instant application. Also, the 1999 Handler et al reference from the Insect Molecular Biology journal has been considered even though it is lined-through on the PTO Form 1449. This was done to avoid duplicate printing of the same reference on the face of any patent to issue from the instant application. The Handler et al reference will be referenced on the face of any issued patent as cited by the Examiner in the course of examination.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 9-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 9-10 recite the limitation of a transformation "system". The term "system" is not clearly defined in the specification as being limited to a composition of matter and implies methods steps, making it unclear as to what elements in addition to the claimed products may be encompassed by the claims. It would be remedial to amend the claims by deleting the term

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“system” and substituting language that makes clear the types of elements encompassed by the claim.

Claims 1, 10, 12 and 18 are vague and indefinite in that the metes and bounds of the term “promoter region” are unclear. The term is not explicitly defined in the specification and it is unclear what are the functional/structural characteristics specified by the term “promoter region”. For example, would a sequence that is obtained from the vicinity of a promoter element, but which does not comprise a promoter element necessarily read on the recited limitation? Does the term necessarily mean that the “promoter region” comprises promoter and/or enhancer activity? Further, it is unclear if the term encompasses elements that have a minimal sequence identity with a polyubiquitin gene promoter element (e.g. as little as two consecutive nucleotides in common) and which has promoter activity (e.g. a promoter sequence obtained from another gene that has homology to a polyubiquitin promoter element).

Claims 10 and 18 are also vague and indefinite in that it is unclear as the claim is written whether the “promoter region of a polyubiquitin gene” is necessarily present in the vector or not since the claim structure implies that the promoter region may be part of what was deleted from the vector. This is exacerbated in claim 10 which is directed to a “system” where, if the “promoter region” is actually present, it is unclear if it is merely present in the system or must actually be part of the vector.

Claims 2, 11, 13 and 19 comprise the phrase “a piggyBac transposase helper plasmid under heat-shock promoter regulation”. First, it is unclear as written that the transposase helper plasmid *necessarily* comprises a coding sequence for the piggyBac transposase. Secondly, the phrase implies that it is the entire plasmid comprising a transposase gene that is somehow

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“regulated” by the heat-shock promoter. It appears from reading the instant specification that the phrase is meant to specify that the plasmid comprises a transposase gene that is under control of a heat-shock inducible promoter and not that the entire plasmid is somehow under control of the heat-shock promoter. It would be remedial to amend the claim to clearly indicate that the plasmid comprises a transposase coding sequence that is under control of the heat-shock promoter.

Claims 11, 13 and 19 are further indefinite in that they are directed to a vector that “further comprises” a plasmid. It is not clear how a vector can further comprise a plasmid. Does this mean that the vector and plasmid are necessarily part of a single nucleic acid construct, or alternatively, that the vector somehow comprises multiple nucleic acids that aren’t covalently linked (e.g. multiple nucleic acids packaged within a virion)? Upon reading the specification, it appears the phrase may be intended to specify that the transposable element and sequences encoding the corresponding transposase be on the same nucleic acid molecule. It would be remedial to amend the claim language to clearly indicate what structures or combination of structures is encompassed by the rejected claim.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

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international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejected claims are directed to a transformation system containing a vector comprising a piggyBac transposon that has been modified by deletion of "about" 748 basepairs of an internal piggyBac sequence. The vector can further comprise a promoter "region" of a polyubiquitin gene. The system can further comprise a piggyBac transposase helper plasmid under control of a heat-shock promoter. The concepts of a deletion of "about" 748 basepairs and of a promoter "region" of a polyubiquitin gene are not explicitly defined in the specification and can be interpreted to read on any deletion of a piggyBac transposon (e.g. a transposable element comprising just the piggyBac inverted repeats) and to any promoter having any homology to the polyubiquitin gene promoter.

Claims 1-5, 9-19 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,218,185 (henceforth the '185 patent).

The applied reference has a common assignee with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The '185 patent teaches a transformation system comprising two DNAs where the first DNA comprises a non-transposon heterologous DNA sequence inserted between the inverted repeats of a piggyBac transposon and the second DNA encodes a transposase active on the pair of inverted repeats (e.g. a transposase helper plasmid). The first DNA of the invention thus

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encompasses embodiments where at least 748 basepairs are deleted from the piggyBac transposon. Moreover, the non-transposon sequence can be a selectable marker gene encoding a fluorescent protein that is operatively linked to a promoter (e.g. column 8, lines 23-40; claim 24). The second DNA can comprise an inducible heat-shock promoter operably linked to the gene encoding the piggyBac transposase such that the “transposase helper plasmid is under heat-shock promoter regulation”. Thus, the transformation system taught by the ‘185 patent anticipate the broadly recited elements of the rejected claims.

It is noted that a more precisely defined wording with regard to the polyubiquitin promoter would probably obviate the instant grounds of rejection for at least some of the claims over the teachings of the ‘185 patent as the patent does not appear to describe such promoter elements (e.g. at least one sequence encoding a fluorescent protein operatively linked to a polyubiquitin promoter obtained from *Drosophila melanogaster*).

Claims 1-5 and 9-19 are rejected under 35 U.S.C. 102(a) as being anticipated by Handler et al (*Insect Molecular Biology*, Vol. 8, No. 4, pages 449-457, November 1999; see the entire reference).

Handler et al teach the germ line transformation of *D. melanogaster* with piggyBac-derived transformation vectors (e.g. Abstract). Transformation of a vector marked with white and green fluorescent protein under nuclear-nuclear localizing sequence regulation yielded seventy G1 transformants that all expressed GFP (e.g. Figure 3a; Abstract). Use of an hsp70-regulated helper construct expressing the piggyBac transposase increased transformation frequency significantly. The authors teach at least one gene transfer construct where 748 bp of



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piggyBac DNA was deleted from the vector backbone (i.e. pB[Dmw, PUBnisEGFP], see column 1 of page 451).

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5 and 9-19 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 11-17 of copending Application No. 10/101,840. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims of the '840 application are directed to a transformation system comprising a vector having the "identifying characteristics" of a vector comprising SEQ ID NO: 6 wherein the vector contains a piggyBac transposon digested with BglII-HpaI, a promoter region of a polyubiquitin gene and a nuclear localization sequence of an SV40 virus. The vector of the system can further comprise a selectable marker gene (e.g. encoding a fluorescent marker) operatively linked to the polyubiquitin promoter region. The transformation system can further

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comprise a piggyBac transposase helper plasmid under control of heat-shock promoter regulation.

The claims of the instant specification are broader in scope in that the transformation “system” and/or vector of the system comprises “a” nucleotide sequence from a piggyBac transposon that has a fluorescent protein gene operatively linked to a polyubiquitin promoter region. Alternatively, the vector can comprise a piggyBac transposon that is modified by deletion of “about” 748 basepairs of an internal piggyBac sequence. In either case, the more narrowly drawn embodiments of the ‘840 claims are totally encompassed by the instant claims. Thus, the claims of the ‘840 patent necessarily make obvious the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1-5, 9-19 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 11 and 20-26 of U.S. Patent No. 6,218,185. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons.

The claims of the ‘185 patent are directed to a transformation “system” comprising a first DNA comprising a non-transposon heterologous sequence inserted between a pair of inverted repeats of a piggyBac transposon and a second DNA encoding a transposase active on the pair of inverted repeats where the second DNA is incapable of transposition caused by the transposon. A cell comprising the DNAs of the transformation “system” can have the second DNA

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comprising an inducible heat-shock promoter. The heterologous non-transposon sequence of the first DNA can comprise a selectable marker gene (e.g. encoding a fluorescent protein).

The claims of the instant application are directed to a transformation system containing a vector comprising a piggyBac transposon that has been modified by deletion of "about" 748 basepairs of an internal piggyBac sequence. The vector can further comprise a promoter "region" of a polyubiquitin gene. The system can further comprise a piggyBac transposase helper plasmid under control of a heat-shock promoter. The concepts of a deletion of "about" 748 basepairs and of a promoter "region" of a polyubiquitin gene are not explicitly defined in the specification and can be interpreted to read on any deletion of a piggyBac transposon (e.g. a transposable element comprising just the piggyBac inverted repeats) and to any promoter having homology to the polyubiquitin gene promoter. Therefore, the claims of the '185 anticipate and make obvious the claims of the instant application.

Claims 1-5, 9-19 are directed to an invention not patentably distinct from claims 1, 11 and 20-26 of commonly assigned U.S. Patent No. 6,218,185. Specifically, for the reasons listed above, the claims of the '185 patent anticipate and make obvious the instant claims.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302).

Commonly assigned U.S. Patent No. 6,218,185, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this

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issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

### ***Conclusion***

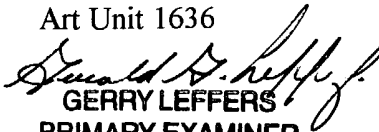
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (571) 272-0772. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gerald G Leffers Jr., PhD  
Primary Examiner  
Art Unit 1636

  
GERRY LEFFERS  
PRIMARY EXAMINER

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